LABORATORY OF TISSUE BIOLOGY AND THERAPEUTIC ENGINEERING
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Université Claude Bernard Lyon 1

PHD PROJECT: 2026-2029

Mechanically-driven mechanisms of osteoarthritis

Name, address of the Host Unit: Tissue Biology and Therapeutic Engineering Laboratory (LBTI), CNRS UMR 5305, 7 passage du Vercors 69367, Lyon cedex 07 and Université Claude Bernard Lyon1
Team ROAD: OsteoArticular and Dental Research (https://lbti.ibcp.fr/)
Supervisor: Jérôme Lafont (assistant professor, cell biology) Jerome.lafont@univ-lyon1.fr
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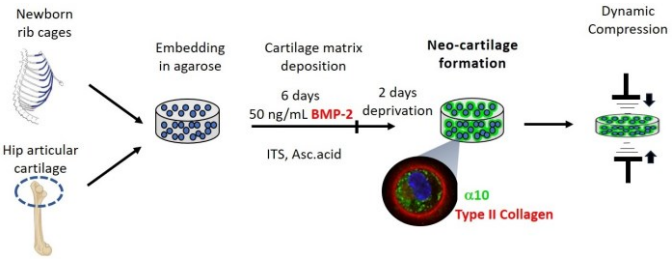
Background: under physiological conditions, articular surfaces are subjected to mechanical stimuli, of which compression is highly represented.
The resident cells of cartilage, the chondrocytes, are surrounded by the pericellular matrix (PCM), which transmits chemical and biomechanical signals to the cells. Abnormal mechanical load of the PCM triggers metabolic changes in chondrocytes causing ECM loss and tissue degeneration, eventually leading to osteoarthritis (OA)[1, 2]. To date, it is still not fully understood how chondrocytes respond to mechanical stimuli in relation to cell signaling[3].
Project: this project aims to better understand how articular chondrocytes respond to mechanical forces and to delineate the role of α-10 Integrin. Although recent studies indicate mechanosensitive ion channels (TRPV4, Piezo-1/2) as crucial responders for mechanical stress, conditional ablation of the encoding genes does not significantly change the severity of OA in a mechanical murine model induced by destabilization of the medial meniscus (DMM). We will investigate the role of integrin α10β1, an integrin receptor most abundantly expressed in cartilage[4], and which could be targeted in skeletal pathologies such as OA. We developped a 3D agarose-based chondrocyte culture allowing us to analyze the effect of dynamic compression on signaling pathways[5,6]. Preliminary results obtained with costal chondrocytes indicate the feasibility for RNAseq and phosphoproteomic studies. We observed a clear differential response of α-10 KO chondrocytes (in collab. with U. of Münich) compared with WT.



Missions and tasks: the mechanically-driven pathways potentially involved in a pathological situation such as OA will now be investigated in a more relevant context by 2 means:
-our validated mechanosensitive system will be used with mouse articular chondrocytes (isolated from hip joint) for transcriptional and phospho-proteomic analyses (i). The mechanical response will be characterized in the presence of α-10 Integrin (normal response) and in the absence of α-10 Integrin.
-then animal model of OA (DMM) will be employed to verify the involvement of the potential candidates previously identified and using spatial omics approaches (ii).
Altogether, the project will uncover new mechanical effectors of compression stress notably through the α-10 Integrin receptor, providing a fundamental understanding of cartilage mechanobiology, and opening new strategies to treat pathologies such as OA.

References

1. Hunter DJ, Bierma-Zeinstra S. *Lancet* 2019;393:1745–1759. **doi**: 10.1016/S0140-6736(19)30417-9.
2. Pettenuzzo S, Arduino A, Belluzzi E, Pozzuoli A, Fontanella CG, Ruggieri P, Salomoni V, Majorana C, Berardo A. Biomedicines. 2023 Jul 8;11(7):1942. doi: 10.3390/biomedicines11071942.
3. Zhao Z, Li Y, Wang M, Zhao S, Zhao Z, Fang J. J Cell Mol Med. 2020 May;24(10):5408-5419. doi: 10.1111/jcmm.15204.
4. Camper L, Holmvall K, Wängnerud C, Aszódi A, Lundgren-Akerlund E. Cell Tissue Res. 2001 Oct;306(1):107-16. doi: 10.1007/s004410100385.
5. Bougault C, Paumier A, Aubert-Foucher E, Mallein-Gerin F. BMC Biotechnol. 2008 Sep 15;8:71. doi: 10.1186/1472-6750-8-71. PMID: 18793425
6. Bougault C, Paumier A, Aubert-Foucher E, Mallein-Gerin F. Nat Protoc. 2009;4(6):928-38. doi: 10.1038/nprot.2009.63. PMID: 19478808